$$DC = \frac{\left(\sum_{i=1}^{n} N_i M_i\right)^2}{\sum_{i=1}^{n} N_i M_i^2 \sum_{i=1}^{n} N_i - \left(\sum_{i=1}^{n} N_i M_i\right)^2}$$

wherein:

n is the number of different molecules in the sample;

N_i is the number of i^{th} molecules in the sample; and

M_i is the mass of the i^{th} molecule.

Please amend claim 7 as follows:

7. (Amended) The mixture according to Claim 1, wherein the **[insulin drug is human insulin and the]** oligomer is covalently coupled to Lys^{B29} of the human insulin **[and has the formula:**

$$\begin{matrix} & \mathbf{O} & \\ & \| & \\ \mathbf{—C—(CH_2)_5—(OC_2H_4)_7—OCH_3]} & & . \end{matrix}$$

Please amend claim 12 as follows:

12. (Amended) **[The mixture according to Claim 1, wherein the insulin drug is insulin]** A mixture of conjugates, each comprising insulin coupled to a first oligomer and a second oligomer, each oligomer covalently coupled to an amine function of the insulin wherein the mixture has a dispersity coefficient (DC) greater than 10,000 where

$$DC = \frac{\left(\sum_{i=1}^{n} N_i M_i\right)^2}{\sum_{i=1}^{n} N_i M_i^2 \sum_{i=1}^{n} N_i - \left(\sum_{i=1}^{n} N_i M_i\right)^2}$$

wherein:

n is the number of different molecules in the sample;

N_i is the number of i^{th} molecules in the sample; and

M_i is the mass of the i^{th} molecule.

Please amend claim 14 as follows:

14. The mixture according to Claim **[13]** 12, wherein the amine function is at Lys^{B29} of the insulin.

Please amend claim 16 as follows:

16. (Amended) The mixture according to Claim **[15]** 12, wherein the first oligomer is covalently coupled at Lys^{B29} of the insulin and the second oligomer is covalently coupled at N-terminal A1 or N-terminal B1 of the insulin.

Please amend claim 18 as follows:

18. (Amended) The mixture according to Claim **[1]** 12, wherein the insulin drug is covalently coupled to at least one of the **[oligomer]** oligomers by a hydrolyzable bond.

Please amend claim 19 as follows:

19. (Amended) The mixture according to Claim **[1]** 12, wherein the insulin is covalently coupled to the polyethylene glycol moiety of at least one of the **[oligomer]** oligomers.

Please amend claim 20 as follows:

20. (Amended) The mixture according to Claim **[19]** 12, wherein at least one of the **[oligomer]** oligomers **[further]** comprises a lipophilic moiety covalently coupled to **[the]** a polyethylene glycol moiety.

Please amend claim 21 as follows:

21. (Amended) The mixture according to Claim **[1]** 12, wherein at least one of the **[oligomer]** oligomers **[further]** comprises a lipophilic moiety.

Please amend claim 25 as follows:

25. (Amended) The mixture according to Claim **[24]** 12, wherein the first and the second oligomers are the same.

Please amend claim 26 as follows:

26. (Amended) The mixture according to Claim **[1]** 12, wherein the oligomer comprises a first polyethylene glycol moiety covalently coupled to the insulin by a non-hydrolyzable bond and a second polyethylene glycol moiety covalently coupled to the first polyethylene glycol moiety by a hydrolyzable bond.

Please amend claim 28 as follows:

28. (Amended) The mixture according to Claim **[1]** 12, wherein the conjugates are each amphiphilically balanced such that each conjugate is aqueously soluble and able to penetrate biological membranes.

Please amend claim 32 as follows:

32. (Amended) The mixture according to Claim 31, wherein the polyethylene glycol moiety has at least 2**[, 3 or 4]** polyethylene glycol subunits.

Please amend claim 33 as follows:

33. (Amended) The mixture according to Claim 31, wherein the polyethylene glycol moiety has at least 5 **[or 6]** polyethylene glycol subunits.

Please amend claim 35 as follows:

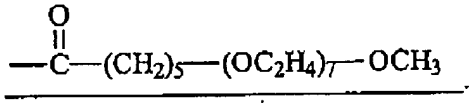
35. (Amended) The mixture according to Claim 31, wherein at least about 96**[, 97, 98 or 99]** percent of the conjugates in the mixture have the same molecular weight.

Please amend claim 38 as follows:

38. (Amended) The mixture according to Claim 31, wherein at least about 96[, 97, 98 or 99] percent of the conjugates in the mixture have the same molecular weight and have the same molecular structure.

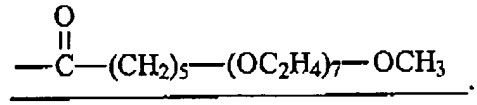
Please amend claim 46 as follows:

46. (Amended) A mixture of conjugates each comprising an insulin drug coupled to an oligomer that comprises a polyethylene glycol moiety, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, wherein the insulin drug is human insulin and each oligomer is covalently coupled to Lys^{B29} of the human insulin and has the formula:



Please amend claim 50 as follows:

50. (Amended) A mixture of conjugates each comprising an insulin drug coupled to an oligomer that comprises a polyethylene glycol moiety, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, in which each conjugate[:] comprises an insulin drug coupled to an oligomer[;] and has the same number of polyethylene glycol subunits, wherein the insulin drug is human insulin and each oligomer is covalently coupled to Lys^{B29} of the human insulin and has the formula:



Please amend claim 53 as follows:

53. (Amended) The mixture according to Claim 52, wherein the polyalkylene glycol **[group]** moiety is a polyethylene glycol moiety.

Please amend claim 54 as follows:

54. (Amended) The mixture according to Claim 53, wherein the polyethylene glycol moiety has at least 2**[, 3 or 4]** polyethylene glycol subunits.

Please amend claim 55 as follows:

55. (Amended) The mixture according to Claim 53, wherein the polyethylene glycol moiety has at least 5 **[or 6]** polyethylene glycol subunits.

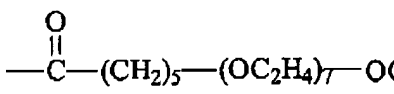
Please add the following new claims:

68. (New) The mixture according to claim 12, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 2 polyethylene glycol subunits.

69. (New) The mixture according to claim 12, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 5 polyethylene glycol subunits.

70. (New) The mixture according to claim 12, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 7 polyethylene glycol subunits.

71. (New) The mixture according to claim 12, wherein at least one of the oligomers is covalently coupled to Lys^{B29} of the human insulin and has the formula:



72. (New) The mixture according to Claim 31, wherein at least about 97 percent of the conjugates in the mixture have the same molecular weight.

73. (New) The mixture according to Claim 31, wherein at least about 98 percent of the conjugates in the mixture have the same molecular weight.

74. (New) The mixture according to Claim 31, wherein at least about 99 percent of the conjugates in the mixture have the same molecular weight.

75. (New) The mixture according to Claim 31, wherein at least about 97 percent of the conjugates in the mixture have the same molecular weight and have the same molecular structure.

76. (New) The mixture according to Claim 31, wherein at least about 98 percent of the conjugates in the mixture have the same molecular weight and have the same molecular structure.

77. (New) The mixture according to Claim 31, wherein at least about 99 percent of the conjugates in the mixture have the same molecular weight and have the same molecular structure.

Please cancel claims 4, 5, 6, 13, 15, 49, and 51 without prejudice or disclaimer for the purpose of incorporating the subject matter of other claims into the claims as discussed below.

Remarks

Claims 1-67 are pending in the present application. Applicants appreciate the indication that claims 40 and 41 are allowed. Applicants further appreciate the indication that claims 7, 16, 49, and 51 contain allowable subject matter.